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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/049,327
Filing Date: May 15, 2002
Appellant(s): MEYTHALER ET AL.

Avery N. Goldstein, PhD
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed May 19, 2010 appealing from the Office action mailed November 24, 2009.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application:

1, 7, 29, 34-36 and 40

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the

subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

5,643,960	Breitner	7-1997
WO 98/20864	Grilli	5-1998

Bustamante et al (Effects of Intrathecal or Intracerebroventricular Administration of Nonsteroidal Anti- inflammatory Drugs on a C-Fiber Reflex in Rats, Journal of Pharmacology and Experimental Therapeutics, 1997, Vol. 281. No.3, pages 1381-1392).

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim 1, 29 and 36 are rejected under 35 U.S.C.112, first paragraph is withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 7, 29, 34-36 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Breitner et al (U.S. Patent 5,643,960) in view of Bustamante et al (Effects of Intrathecal or Intracerebroventricular Administration of Nonsteroidal Anti-inflammatory Drugs on a C-Fiber Reflex in Rats, Journal of Pharmacology and Experimental Therapeutics, 1997, Vol. 281. No.3, pages 1381-1392) and Grilli (WO 98/20864), all of the references are of record.

Breitner teaches a method of delaying the onset of Alzheimer's disease or related neurodegenerative disorders associated with excitotoxic neuronal cell death (for example, Huntington's disease, amyotrophic lateral sclerosis, epilepsy, Parkinson's disease, and Pick's disease). The method comprises administering to an individual at risk of developing the disease (or disorder) an amount of a nonsteroidal anti-inflammatory agent (column 3, lines 7-14). Breitner teaches that the Nonsteroidal anti-

inflammatory agents suitable for use in the present invention include the arylcarboxylic acids (salicylic acid, acetylsalicylic acid, diflunisal, choline magnesium trisalicylate, salicylate (column 3, lines 39). Breitner teaches that all of these NSAIDs are potent inhibitors of cyclooxygenase (COX) (column 3, line 51-52).

Breitner does not expressly teach administering NSAIDs intrathecally or intraventricularly, and further administering a deacetylated aspirin (an active metabolite of aspirin) for the treating of Alzheimer's disease associated with neuronal cell death.

Bustamante teaches a method of administering intrathecally aspirin with a dosage range from 10tJg to 500tJg and other NSAIDs with a dosage range from 100tJg to 500tJg (table 1) (page 1383). Bustamante teaches a method of administering intracerebroventricularlly aspirin with a dosage of 500 tJg and NSAIDs with a dosage of 250 or 500tJg (table 1) (page 1383).

Grilli et al. teaches the treatment of Alzheimer's disease through the use of NSAIDs (Abstract). Sodium salicylate and salicylamide are specifically taught as NSAIDs useful in the invention disclosed therein (page 3, lines 1-10). Neuronal damages (i.e. neurotrauma or neuronal injury) related to Alzheimer's disease, Parkinson's disease, spinal traumas and cranial traumas as well as other neurodegenerative processes are specifically taught as treatable by the NSAIDs disclosed therein (page 6, lines 9-20). Grilli et al. teach, on page 5, lines 1-10, that non-

steroidal anti-inflammatory drugs can be used in the prevention and/or treatment of glutamate receptor-mediated neuronal damages, independently of any anti-inflammatory properties. Grilli et al teaches that a preferred embodiment is the use of ASA or of it's rnetabolite (e.g., deacetylated aspirin), for the treatment of glutamate receptor-mediated neuronal damages (page 3, lines 11-14). Further the NSAIDs show a protective activity against glutamate-induced neurotoxicity.

It would have been obvious to one of ordinary skill in the art at the time of the invention was made to modify the teachings of Breitner to include the administration of NSAIDs intrathecally or intraventricularly. One would be motivated to make such a modification because anti-inflammatory agents and aspirin may be administered intrathecally and intracerebroventricularlly as taught by Bustamante. The amounts of active agents to be used, the pharmaceutical forms, e.g., tablets, etc; mode of administration, flavors, surfactant are all deemed obvious since they are all within the knowledge of the skilled pharmacologist and represent conventional formulations and modes of administration. Furthermore, no unobviousness is seen in the ratio claimed because once the usefulness of a compound is known to treat a condition, it is within the skill of the artisan to determine the optimum ratio.

It would have been obvious to one of ordinary skill in the art at the time of the invention was made to incorporate deacetylated aspirin in the method of Breitner to treat Alzheimer's disease associated with neuronal injuries because it is known in the

art that non-steroidal anti-inflammatory drugs can be used in the treatment of glutamate receptor-mediated neuronal damages, independently of any anti-inflammatory properties as taught by Grilli. One of ordinary skill in the art would have been motivated to make such a modification because employing any known NSAID, including ASA or of it's metabolite (i.e., deacetylated aspirin), for the treatment of neuronal damages as taught in Breitner would be reasonably expected to be effective. At least additive effect is expected.

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

(10) Response to Argument

Appellants submit that a person of ordinary skills in the art has ample guidance concerning how to make and use a progdrugs of CMT and that the specification discloses several examples of prodrugs. This argument has been fully considered and has been found persuasive. Therefore, the rejection under 35 U.S.C. 112, first paragraph has been withdrawn.

Appellants argue that Breitner is not cited as neurotrauma with CMT. And that is no suggestion that any NSAIDS may be used as such. This argument has been fully considered but are not convincing. Breitner teaches that the Nonsteroidal anti-inflammatory agents suitable for delaying the onset of **Alzheimer's disease or related neurodegenerative disorders** associated with excitotoxic neuronal cell death (for example, Huntington's disease, amyotrophic lateral sclerosis, epilepsy, Parkinson's disease, and Pick's disease). In the present invention include the arylcarboxylic acids (**salicylic acid, acetylsalicylic acid**, diflunisal, **choline magnesium trisalicylate**, salicylate (column 3, lines 39). And Breitner teaches that all of these NSAIDs are potent inhibitors of cyclooxygenase (COX). And Bustamante teaches a method of administering intrathecally aspirin with a dosage range from 10µg to 500µg and other NSAIDs with a dosage range from 100µg to 500µg (table 1) (page 1383). Grilli et al. teaches the treatment of Alzheimer's disease through the use of NSAIDs (Abstract). Sodium salicylate and salicylamide are specifically taught as NSAIDs useful in the invention disclosed therein (page 3, lines 1-10). Neuronal damages (i.e. neurotrauma or neuronal injury) related to Alzheimer's disease, Parkinson's disease, spinal traumas and cranial traumas as well as other neurodegenerative processes are specifically taught as treatable by the NSAIDs disclosed. It would have been obvious to administer CMT for delaying the onset of Alzheimer's disease or related neurodegenerative disease as taught by Breitner and to further employ deacetylated aspirin for the treatment of Alzheimer's disease associated with neuronal injuries because it is known in the art that non-steroidal anti-inflammatory drugs can be used in the treatment of

glutamate receptor-mediated neuronal damages, independently of any anti-inflammatory properties as taught by Grilli.

Appellants argue that the unsupported statement in Grilli that ASA of NaSal are effective treatment of Alzheimer's disease does not lead one of ordinary skill in the art to other NSAIDs or specifically to CMT for the treatment of neurotrauma or neuronal injury. No teaching of Grilli provides any reasonable expectation that CMT will more like ASA or NaSal than indomethacin. This argument has been fully considered but are not convincing. Grilli et al. teaches the treatment of Alzheimer's disease through the use of NSAIDs (Abstract). Sodium salicylate and salicylamide are specifically taught as NSAIDs useful in the invention disclosed therein (page 3, lines 1-10). Neuronal damages (i.e. neurotrauma or neuronal injury) related to Alzheimer's disease, Parkinson's disease, spinal traumas and cranial traumas as well as other neurodegenerative processes are specifically taught as treatable by the NSAIDs disclosed therein (page 6, lines 9-20). Grilli et al. teach, on page 5, lines 1-10, that non-steroidal anti-inflammatory drugs can be used in the prevention and/or treatment of glutamate receptor-mediated neuronal damages, independently of any anti-inflammatory properties. Grilli et al teaches that a preferred embodiment is the use of ASA or of it's rnetabolite (e.g., deacetylated aspirin), for the treatment of glutamate receptor-mediated neuronal damages (page 3, lines 11-14). It would have been obvious to one of ordinary skill in the art at the time of the invention was made to incorporate deacetylated aspirin in the method of Breitner to treat Alzheimer's disease associated with neuronal injuries because it is known in the art that non-steroidal anti-

inflammatory drugs can be used in the treatment of glutamate receptor-mediated neuronal damages, independently of any anti-inflammatory properties as taught by Grilli. One of ordinary skill in the art would have been motivated to make such a modification because employing any known NSAID, including ASA or of it's metabolite (i.e., deacetylated aspirin), for the treatment of neuronal damages as taught in Breitner would be reasonably expected to be effective. At least additive effect is expected.

Appellants argue that Bustamante merely teaches intrathecal administration of some NSAIDs. And Bustamante fails to bolster the deficiencies of Breitner and Grilli. This argument has been fully considered but are not convincing. Bustamante teaches a method of administering intrathecally aspirin with a dosage range from 10tJg to 500tJg and other NSAIDs with a dosage range from 100tJg to 500tJg (table 1) (page 1383). Bustamante teaches a method of administering intracerebroventricularlly aspirin with a dosage of 500 tJg and NSAIDs with a dosage of 250 or 500tJg (table 1) (page 1383). Breitner teaches that the Nonsteroidal anti-inflammatory agents suitable for delaying the onset of **Alzheimer's disease or related neurodegenerative disorders** associated with excitotoxic neuronal cell death (for example, Huntington's disease, amyotrophic lateral sclerosis, epilepsy, Parkinson's disease, and Pick's disease). In the present invention include the arylcarboxylic acids (**salicylic acid, acetylsalicylic acid**, diflunisal, **choline magnesium trisalicylate**, salicylate (column 3, lines 39). And Breitner teaches that all of these NSAIDs are potent inhibitors of cyclooxygenase (COX). Grilli et al. teaches the treatment of Alzheimer's disease through the use of NSAIDs (Abstract). Sodium salicylate and salicylamide are specifically taught as

NSAIDs useful in the invention disclosed therein (page 3, lines 1-10). Neuronal damages (i.e. neurotrauma or neuronal injury) related to Alzheimer's disease, Parkinson's disease, spinal traumas and cranial traumas as well as other neurodegenerative processes are specifically taught as treatable by the NSAIDs disclosed. It would have been obvious to administer CMT for delaying the onset of Alzheimer's disease or related neurodegenerative disease as taught by Breitner and to further employ deacetylated aspirin for the treatment of Alzheimer's disease associated with neuronal injuries because it is known in the art that non-steroidal anti-inflammatory drugs can be used in the treatment of glutamate receptor-mediated neuronal damages, independently of any anti-inflammatory properties as taught by Grilli. It would have been obvious to one of ordinary skill in the art at the time of the invention was made to modify the teachings of Breitner to include the administration of NSAIDs intrathecally or intraventricularly. One would be motivated to make such a modification because anti-inflammatory agents and aspirin, which are known in the art to be effective agents in the treatment of neurotrauma or neurodegenerative disease as taught by Breitner and Grilli, may be administered intrathecally and intracerebroventricularlly as taught by Bustamante.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/San-ming Hui/

Primary Examiner, Art Unit 1628

Conferees:

/KATHRIEN CRUZ/

Examiner, Art Unit 1628

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627